

Sleep Changes and Sleep-Related Disorders in the Elderly

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Sleep Facts

- More than 50% of geriatric patients report difficulty sleeping
- Insomnia is not defined by the sleep lost each night, but by the drowsiness, difficulty concentrating, headaches, irritability, and other problems it causes each day
- Adults who get less than 7 hours of sleep/night on a regular basis are more likely to have diabetes, asthma, or cancer
- Over 70 million Americans (22%) suffer some kind of sleep disorder, of those, over 60% have a chronic sleep disorder
- Almost everything we know about sleep was discovered in the last 30 years

Normal Sleep Structure and Physiology

Sleep Architecture

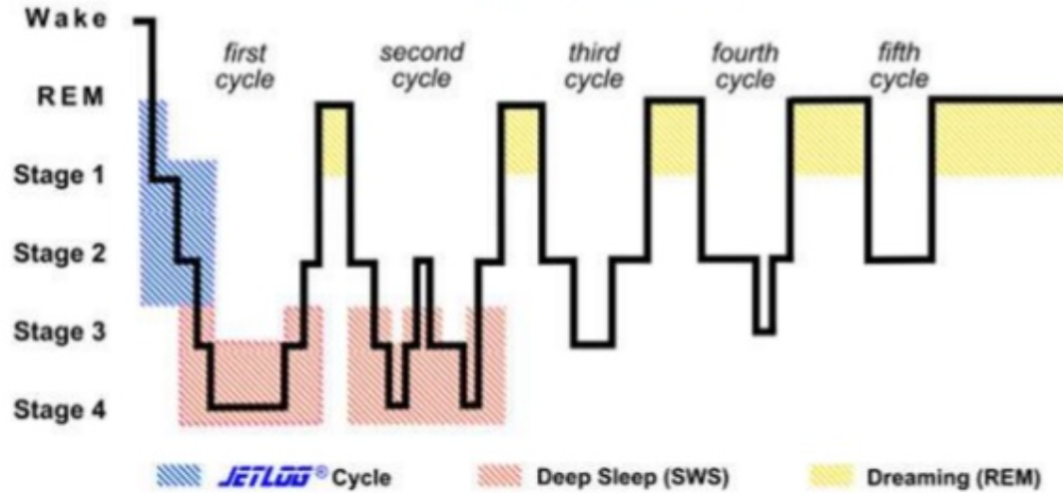
There are 2 types of sleep

1. Non-rapid eye movement (NREM)
 - a. Divided into stages 1, 2, 3, and 4
2. Rapid eye-movement (REM)

A sleep episode begins with a short period of NREM stage 1, then progressing through stage 2, 3, and 4 and finally to REM.

Over the course of a period of sleep, NREM and REM sleep alternate cyclically.

Sleep Stages



NREM = 75-80% of total time spent in sleep

<https://www.slideshare.net/ashrafeladawy/normal-sleep-architecture>

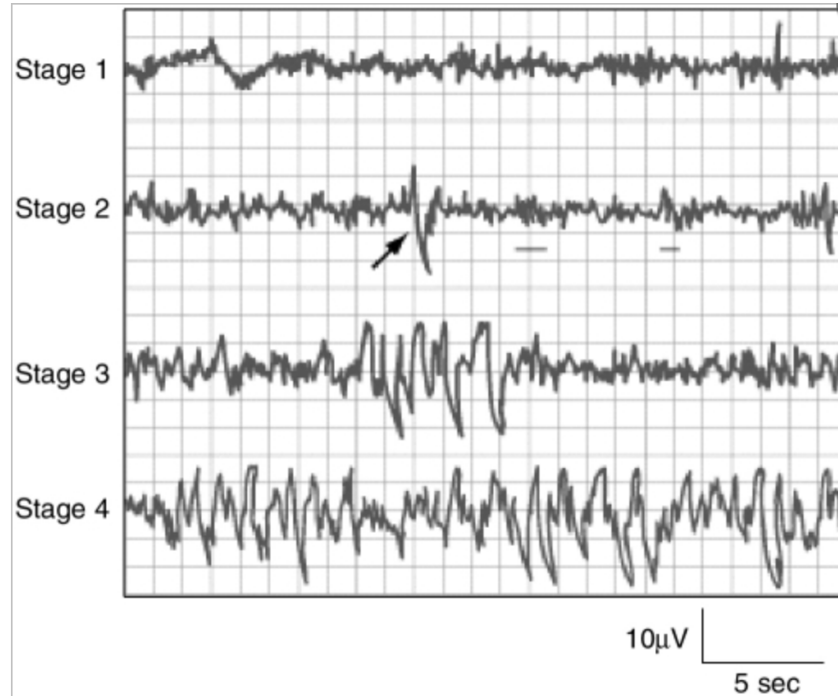
REM = 20-25% of total time spent in sleep

Average length of 1st sleep is 70 to 100 minutes, later cycles are longer lasting at about 90 to 120 minutes

REM sleep increases as the night progresses

As the sleep episode progresses, stage 2 begins to account for the majority of NREM sleep, and stages 3 and 4 may altogether disappear

Four Stages of NREM Sleep



<https://www.ncbi.nlm.nih.gov/books/NBK19956/figure/200007efmm00004/report/objectivity>

1. Stage 1
2. Stage 2
3. Stage 3 and 4, Slow-Wave Sleep

REM Sleep

- REM sleep is defined by the presence of desynchronized brain wave activity, muscle atonia, loss of reflexes, and bursts of rapid eye movements
- During initial cycle, REM lasts 1-5 minutes, becomes progressively prolonged as sleep episode progresses
- Dreaming is most often associated with REM sleep
- REM sleep may be important for memory consolidation

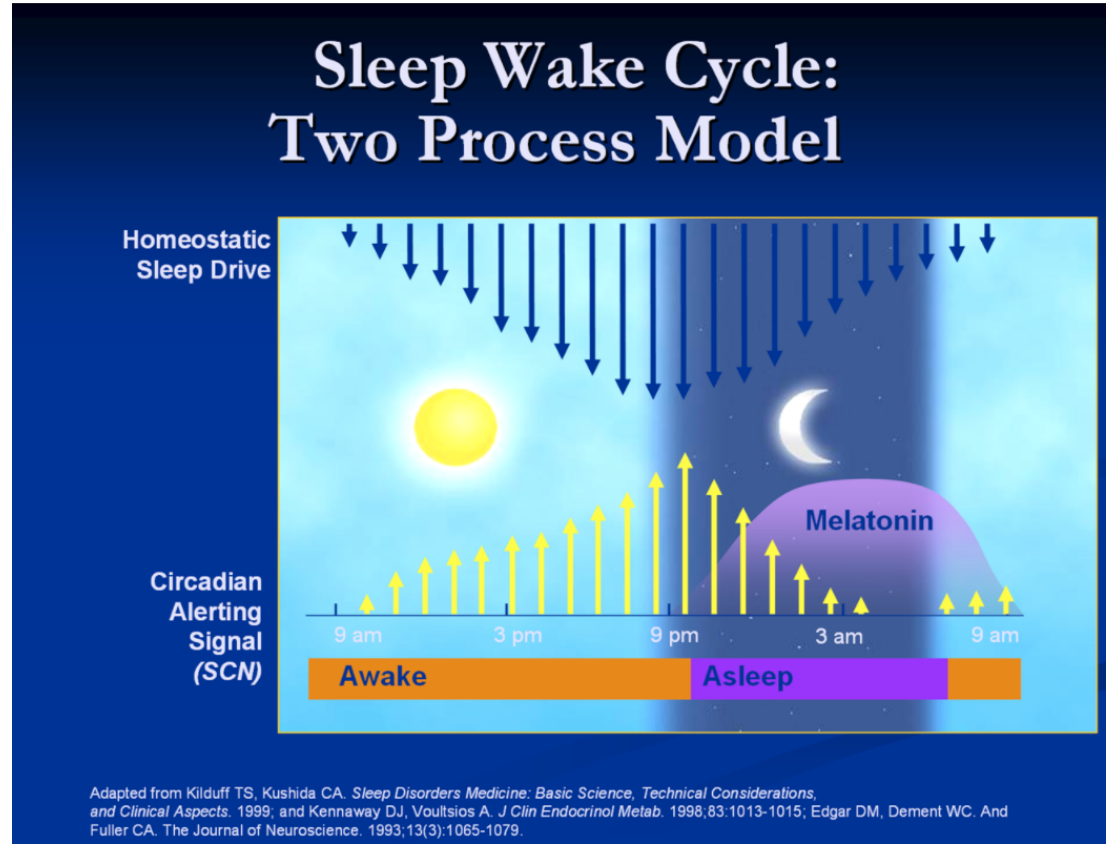


Physiological Changes During Sleep

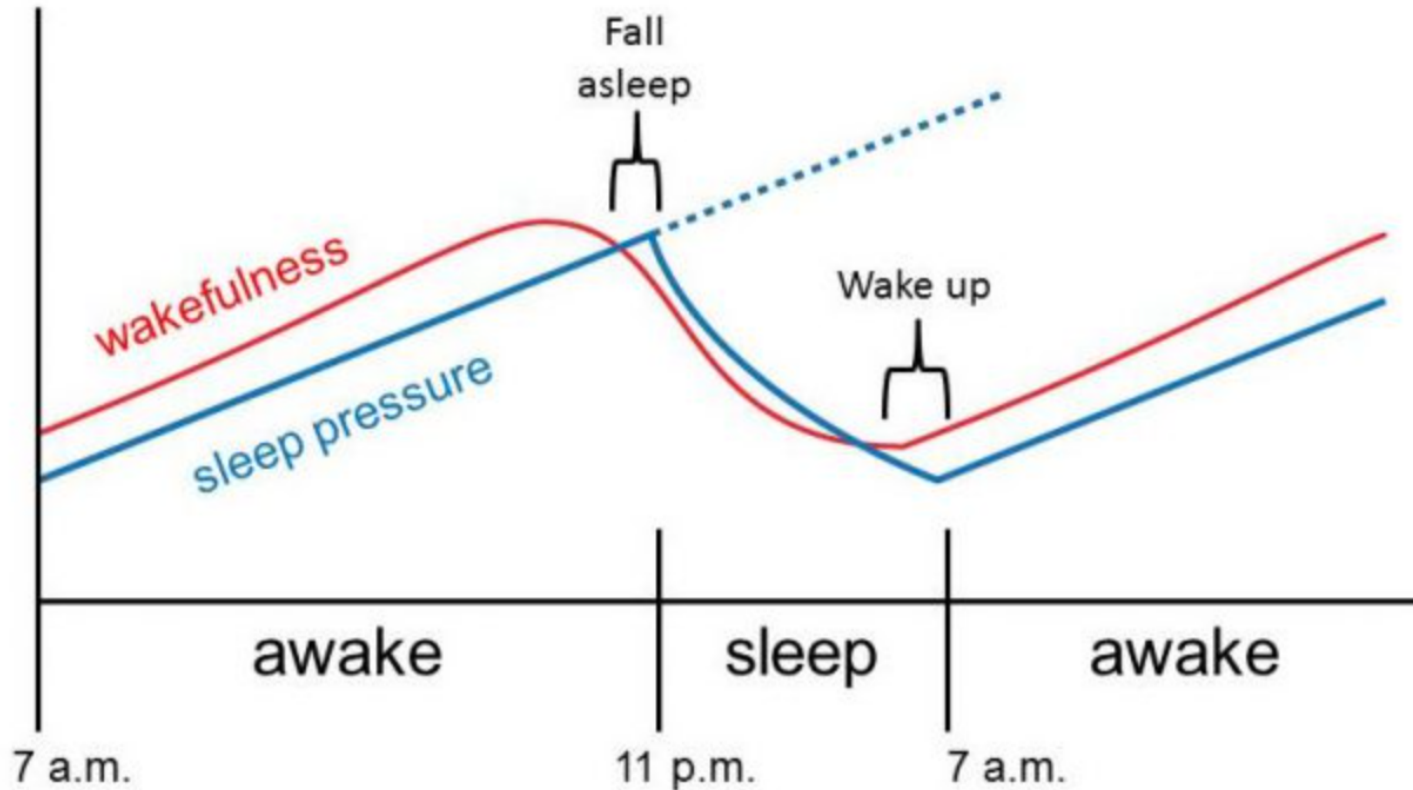
| Physiological Process | NREM | REM |
|----------------------------|--|---|
| Brain activity | Decreases from wakefulness | Increases in motor and sensory areas, while other areas are similar to NREM |
| Heart rate | Slows from wakefulness | Increases and varies compared to NREM |
| Blood pressure | Decreases from wakefulness | Increases (up to 30 percent) and varies from NREM |
| Sympathetic nerve activity | Decreases from wakefulness | Increases significantly from wakefulness |
| Muscle tone | Similar to wakefulness | Absent |
| Blood flow to brain | Decreases from wakefulness | Increases from NREM , depending on brain region |
| Respiration | Decreases from wakefulness | Increases and varies from NREM , but may show brief stoppages; coughing suppressed |
| Airway resistance | Increases from wakefulness | Increases and varies from wakefulness |
| Body temperature | Is regulated at lower set point than wakefulness; shivering initiated at lower temperature than during wakefulness | Is not regulated; no shivering or sweating; temperature drifts toward that of the local environment |
| Sexual arousal | Occurs infrequently | Greater than NREM |

Two Major Sleep Regulatory Systems

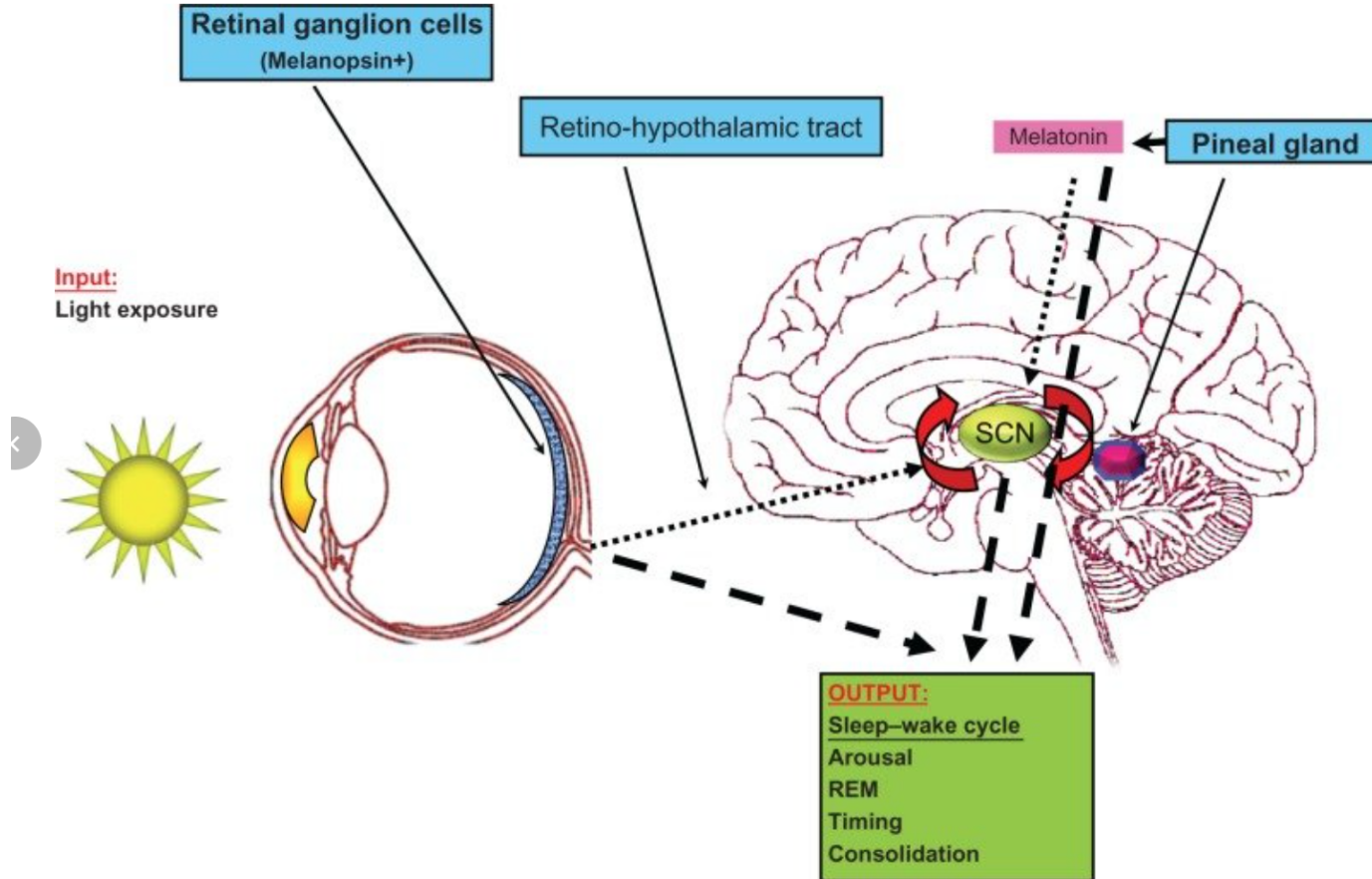
1. Homeostatic sleep-wake process - regulates the intensity of sleep
2. Circadian timing system - regulates the timing of sleep

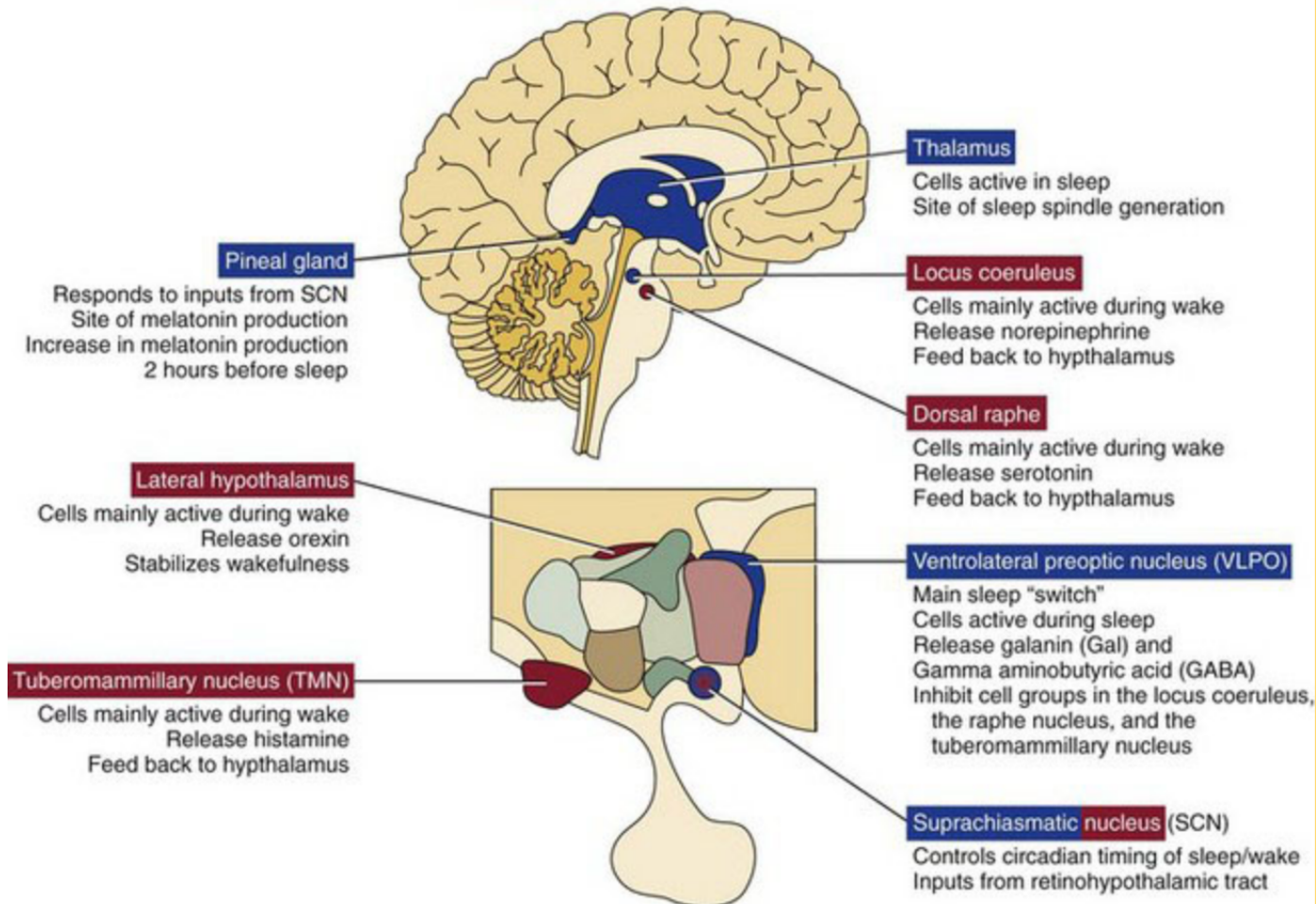


Synchronization of Homeostatic and Circadian Processes



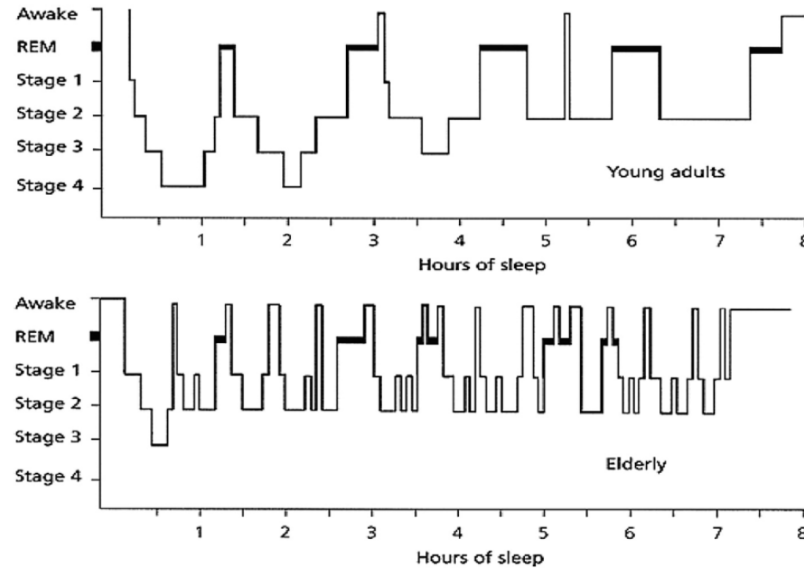
More About the Circadian Timing System





Changes in Sleep Structure and Physiology in the Elderly

Sleep Structure Changes in the Elderly



- With aging, there is an increase in the duration of stage 1 sleep and in the number of shifts into stage 1 = fragmentation of sleep
- Stages 3 and 4 (SWS) decrease with age and in extreme old age (>90) may disappear completely = less deep sleep and more likely to woken up by auditory stimuli

Circadian Rhythm Changes in the Elderly

- Advance of timing of sleep to earlier hours
- Reduced circadian rhythm amplitude
- Age-related changes in the pathway through the eye, such as yellowing of the lens, is associated with greater reported sleep disturbances
- Strong evidence of altered patterns of electrical activity in the SCN

What does all this mean?

- Time in bed: increased
- Total sleep period: increased
- Total sleep time: reduced or unchanged
- Sleep latency: variable, but seems to be more increased
- Wake after sleep onset: increased
- Sleep efficiency: decreased

Despite these changes, excessive daytime somnolence is not part of normal aging!

Older people may spend more time in bed to get the same amount of sleep as when they were younger, and have daytime napping, but total sleep time is only slightly decreased

Box 1: Typical sleep changes with aging

- Decreased total nocturnal sleep time
- Delayed onset of sleep
- Advanced circadian phase: early to bed, early to rise
- Reduced slow-wave sleep
- Reduced rapid-eye-movement (REM) sleep
- Reduced threshold for arousal from sleep
- Fragmented sleep with multiple arousals
- Daytime napping

Assessing Sleep and Sleep Hygiene

Questions to Ask Patient About Sleep

Suggested Questions About Sleep and Sleepiness

How has the patient been sleeping recently?

When did the problem begin? (To differentiate between acute and chronic insomnia)

Does the patient have a psychiatric or medical condition that may cause insomnia? (May relate to an underlying condition that should be treated first)

Is the sleep environment conducive to sleep? (Noise, interruptions, temperature, light)

Does the patient report "creeping, crawling or uncomfortable feelings" in the legs that are relieved by moving the legs? (May relate to restless legs syndrome)

Does the bed partner report that the patient's legs or arms jerk during sleep? (May relate to periodic limb movements in sleep)

Does the patient snore loudly, gasp, choke or stop breathing during sleep? (May relate to obstructive sleep apnea)

Is the patient a shift worker? What are the work hours? Is the patient an adolescent? (May relate to circadian sleep disorders/sleep deprivation)

What are the bedtimes and rise times on weekdays and weekends? (May relate to poor sleep hygiene)

Does the patient use caffeine, tobacco or alcohol? Does the patient take over-the-counter or prescription medications (such as stimulating antidepressants, steroids, decongestants, beta blockers)? (May relate to substance-induced insomnia)

What daytime consequences does the patient report? (Daytime consequences may be significant)

Does the patient report dozing off or having difficulty staying awake during routine tasks, especially while driving? (This is a serious problem that should be dealt with promptly)

Helpful to keep sleep diary for 1-2 weeks:

- Record bedtime
- Total sleep time
- Time until sleep onset
- Number of awakenings
- Use of sleep medications
- Time out of bed in the AM
- Rating of quality of sleep
- Daytime symptoms

Medications, Medications, Medications

Medications associated with insomnia

| Type | Medications |
|-------------------|---|
| Antidepressants | SSRIs (Fluoxetine), SNRI (Venlafaxine), Bupropion, MAOI |
| Antipsychotics | Aripiprazole |
| Stimulants | Methylphenidate, Modafinil, Caffeine, Amphetamine |
| Antihypertensives | Beta blockers, Amlodipine, Diltiazem, Verapamil, Methyldopa |
| Bronchodilators | Theophylline, albuterol |
| Corticosteroids | Prednisone, Dexamethasone |
| Decongestants | Pseudoephedrine, Phenylephrine, Phenylpropanolamine |

Praharaj, Samir Kumar, Ravi Gupta, and Navendu Gaur. "Clinical Practice Guideline on Management of Sleep Disorders in the Elderly." *Indian Journal of Psychiatry* 60, no. Suppl 3 (February 2018): S383–96. <https://doi.org/10.4103/0019-5545.224477>.

Table 2: Medications and other substances that can contribute to insomnia in older patients

| Substance | Effects and points of advice |
|-------------------------------|---|
| Alcohol | Sleep induction Subsequent sleep disruption |
| Anticholinesterase inhibitors | Insomnia Disturbing dreams |
| β-blockers | Sleep physiology altered Nightmares possible |
| Caffeine, decongestants | Stimulant effects • Advise patient to avoid evening use |
| Carbadopa, levadopa | Nightmares; insomnia |
| Corticosteroids | Stimulant effect; may cause agitation • Prescribe lowest possible dose |
| Diuretics | Nocturia • Avoid late in day |
| Nicotine | • Encourage smoking cessation |
| Phenytoin (e.g., Dilantin) | Frequent insomnia |
| SSRIs | Frequent insomnia |
| Theophylline | Stimulant effect • Substitute metered-dose bronchodilators |
| Thyroid hormone | • Check thyroid function |

Note: SSRIs = selective serotonin reuptake inhibitors.

Medical Conditions Contributing to Insomnia

Medical conditions associated with insomnia in elderly

| Medical conditions | |
|--------------------|---|
| Cardiovascular | Arrhythmia, Congestive cardiac failure, Myocardial infarction |
| Pulmonary | Chronic obstructive pulmonary disease, Asthma |
| Neurological | Dementia, Stroke, Brain injury |
| Endocrine | Type 2 Diabetes mellitus, Hypothyroidism |
| Musculoskeletal | Osteoarthritis, Fibromyalgia, Kyphosis |
| Urological | Benign prostatic hyperplasia, Prostate cancer |
| Renal | Chronic kidney disease, End-stage renal disease |
| Gastrointestinal | Gastroesophageal reflux disease, Irritable bowel syndrome |
| Other | Cancer, Menopause, Bruxism |

Psychiatric Disorders Contributing to Insomnia

Insomnia in psychiatric disorders

| Disorder | Sleep changes | PSG findings |
|------------------------|---|---|
| Depression | Sleep onset and maintenance insomnia, early morning awakening (hypersomnia in atypical depression) | Prolonged sleep latency, decreased sleep efficiency, short REM latency, increased percent REM sleep, increased REM density, decreased slow-wave sleep |
| Bipolar disorder | <i>Manic phase:</i> decreased sleep need (short sleep) <i>Depressive phase:</i> hypersomnia (40-80%) or insomnia | Longer sleep onset latency, poorer sleep efficiency, reduced sleep period time, increased percentage of stage 1 sleep, shortened REM latency, and increased REM density |
| Anxiety disorder | Initial insomnia, ruminations | Increased sleep latency, decreased sleep efficiency, increased stage N1 and N2 sleep, decreased slow-wave sleep, decreased REM sleep, shortened total sleep time |
| Schizophrenia | Sleep onset and maintenance insomnia | Prolonged sleep latency, decreased sleep efficiency, poor subjective sleep quality, shorter total sleep time, and disrupted circadian rhythmicity |
| Substance use disorder | Sleep onset and maintenance insomnia | Alcohol withdrawal: increased N1 sleep, decreased slow-wave sleep, shortened REM latency, increased REM sleep percent |

Assessment Tools

Objective assessment scales in insomnia

| Scale | Description |
|---|--|
| Insomnia severity index (ISI) | A 7-item instrument to measure the severity of insomnia. Scores 0-7 is no insomnia, 8-14 subthreshold insomnia, 15-21 clinical insomnia – moderate, and 22-28 clinical insomnia – severe. Hindi version is available. |
| Pittsburgh Sleep Quality Index (PSQI) | A 19-item scale with seven subscales (subjective sleep quality, sleep latency, sleep duration, habitual sleep disturbances, use of sleep medication and daytime dysfunction); each of which is rated from 0–3. Higher scores reflect more severe sleep complaints. |
| Epworth Sleepiness Scale (ESS) | A self-rated questionnaire with 8-items that assesses the chances of falling asleep or dozing off while doing eight different activities. It is rated on a 4-point scale (0-3) and the total score can range from 0 to 24. Higher ESS score denotes the average sleep propensity in daily life, i.e. daytime sleepiness. |
| Dysfunctional Beliefs and Attitudes about Sleep Questionnaire (DBASQ) | A self-rated instrument with 28 items that measure negative cognitions about sleep. A Hindi version, DBAS-16 is available. |

Sleep Hygiene

General Sleep Hygiene Measures

Sleep hygiene measures may help promote sleep. Sleep hygiene measures relate to health practices and environmental influences on sleep:

Wake up at the same time each day.

Discontinue caffeine intake four to six hours before bedtime and minimize total daily use. Caffeine is a stimulant and may disrupt sleep.

Avoid nicotine, especially near bedtime and on night awakenings. It is also a stimulant.

Avoid the use of alcohol in the late evening to facilitate sleep onset. Alcohol can cause awakening later in the night.

Avoid heavy meals too close to bedtime, since this may interfere with sleep. A light snack may be sleep-inducing.

Regular exercise in the late afternoon may deepen sleep. Vigorous exercise within three to four hours of bedtime may interfere with sleep.

Minimize noise, light and excessive temperatures during the sleep period.

Move the alarm clock away from the bed if it is a source of distraction.

Sleep-Related Pathology in the Elderly

- Types of Insomnia
- Disorders to Rule Out
 - Obstructive Sleep Apnea
 - Restless Leg Syndrome
 - Rapid Eye Movement Disorder
 - Circadian Rhythm Sleep-Wake Disorders

Definition of Insomnia

- An experience of inadequate or poor-quality sleep characterized by 1 or more of the following:
 - Difficulty falling asleep, difficulty maintaining sleep, waking up too early in the morning, sleep that is not refreshing
- Involves daytime consequences such as fatigue, lack of energy, difficulty concentrating, and irritability

Classification of Insomnia

- Transient insomnia: no more than a few nights
- Acute insomnia: less than 3-4 weeks
- Chronic insomnia: more than 3-4 weeks



Impact of Sleep Impairment

- Physically and mentally fatigued, anxious, irritable
- As bedtime approaches, insomniacs become more tense, anxious, worried about health, death, work, and personal problems
- Increases risk of accidents, malaise, chronic fatigue
- Decreased memory and concentration, impaired performance on psychomotor tests, increased risk of falls, cognitive decline, higher mortality rate



Nonpharmacologic Therapies

- Sleep hygiene should be tailored and applied to every patient
- Adjusting the dose and timing of medication administration
- Set reasonable expectations and explain how anxiety leads to a vicious cycle
- If minimal or no impairment in daytime functioning, patient may simply need reassuring that the symptoms are not pathological or damaging

Table 3 Sleep-Hygiene Measures

| |
|---|
| Avoid and minimize use of caffeine, cigarettes, stimulants, alcohol, and other medications |
| If medically able, increase activity level in the afternoon or early evening (not close to bedtime) by walking or exercising outdoors |
| Increase exposure to natural light and bright light during day and early evening |
| Avoid napping, particularly after 2:00 PM; limit naps to 1 nap of less than 30 minutes |
| Check the effect of medications on sleep |
| Go to bed only when sleepy |
| Maintain comfortable temperature in bedroom |
| Minimize light and noise exposure as much as possible |
| Eat a light snack if hungry |
| Avoid heavy meals at bedtime |
| Limit liquids in the evening |
| Keep a regular schedule |
| Rest and retire at the same time each day |
| Eat and exercise on a regular schedule |
| Stress-management measures: |
| Tolerance of occasional sleeplessness |
| Discuss worries and stressful events enough time before bedtime |
| Use relaxation techniques |

Behavioral Therapies

- Aim is to change maladaptive sleep habits, reduce autonomic arousal, alter dysfunctional belief and attitudes that can perpetuate insomnia
- Relaxation therapy
- Sleep restriction therapy
- Stimulus-control therapy
- Cognitive therapy
- Bright light therapy



Role of Pharmacological Therapies

5 basic principles characterize rational pharmacotherapy for insomnia:

1. Use the lowest effective dose
2. Use intermittent dosing (2 to 4 times weekly)
3. Short-term medication prescribing (regular use for not more than 3 to 4 weeks)
4. Gradual medication discontinuation to reduce rebound insomnia
5. Medications with shorter elimination half-lives are generally preferred to minimize daytime sedation

Benzodiazepines

- Improve insomnia by reducing REM sleep, decreasing sleep latency, decreasing nocturnal awakenings
- Absorption not affected by aging
- Decrease in lean body mass, reduction in plasma proteins, and increase in body fat seen in older adults result in an increased concentration of unbound drug and increased drug-elimination half-life
- Long-acting BZDs should be avoided
- Rebound insomnia can occur within 1-2 weeks of use, hangover effects, impair psychomotor performance and memory, tolerance develops quickly, addiction, daytime sedation, dizziness, falls, hip fractures, car accidents
- Bottom line: avoid in the elderly

Non-Benzodiazepine Medications

- Zolpidem (Ambien)
 - Used for sleep-onset
 - Short half-life of 2.5 to 2.9 hours
 - Contraindicated in sleep-related breathing disorders, severe hepatic impairment, acute pulmonary impairment, respiratory depression
 - Well tolerated in the elderly
 - Most common side effects: nausea, dizziness, drowsiness, rebound insomnia
 - Has not been associated with hangover effects or tolerance
 - Does not alter sleep architecture
 - Patients can become dependent with use more than 4 weeks
 - There is sustained-release formulation that can be used for sleep maintenance

- **Zaleplon (Sonata)**
 - Used for sleep-onset insomnia
 - Can be used specifically for treatment of midnight awakenings because its short half-life
 - Half-life of 1 hour
 - No major side effects have been reported
 - Demonstrated safety and efficacy in older adults during short and long-term treatment
 - No tolerance, rebound insomnia, or withdrawal symptoms



- Eszopiclone (Lunesta)

- Randomized double-blinded study by Scharf, including 231 elderly patients (mean age 72) showed that eszopiclone significantly improved sleep latency, quality and depth of sleep, increased total sleep time, and reduced wake time after sleep onset ($P < 0.05$)
- Reduced the number and duration of naps
- Half-life of 6 hours, may be used for sleep maintenance
- Most common side effect was headache
- Meta-analysis of 5 randomized-controlled trials demonstrated safety and efficacy in the elderly



Antidepressants

- Trazodone
 - Non-tricyclic antidepressant with sedative properties
 - Half-life of 10 to 12 hours
 - Reported to increase slow wave sleep
 - Often used to treat depressed patients with significant insomnia; but therapeutic efficacy in non-depressed patients is unknown
 - Review of 58 studies, in which 1621 patients received trazodone at doses of 75 to 500mg, most common side effects were: drowsiness, tiredness, GI effects, dizziness, dry mouth, insomnia, headache, hypotension, agitation, tachycardia
 - American Academy of Sleep Medicine recommends that trazodone not be used for sleep onset or maintenance because harms outweigh the benefits

- Doxepin
 - Only FDA approved antidepressant for insomnia at doses 3 to 6mg
 - Tricyclic antidepressant and is selective for histamine 1 receptors
 - Studies of patients 65 years and older with doses 1mg and 3mg have shown significantly improved measures of sleep onset, sleep duration, sleep quality over a 12-week period
 - Improvements sustained for long duration of 3 months
 - Not associated with tolerance or anticholinergic side effects or cardiac repolarization
 - No risk of addiction or dependence
 - No incidence of withdrawal symptoms or rebound insomnia after discontinuation
 - No residual symptoms the next day

- Mirtazapine
 - Strong 5-HT₂ antagonism
 - In a study of adults age 18 to 75 years old (mean age 40.9), the mirtazapine group had significant improvement in sleep latency, sleep efficiency, and awakenings after sleep onset after 2 weeks of treatment
 - Because of conflicting evidence and habituation to its sedative effects, it should not be used to treat insomnia in the absence of depression

- MT1/MT2 Receptor Agonist

- Ramelteon approved by FDA for treatment of chronic insomnia in the elderly
- A randomized, double-blind study included 829 patients (mean age 72) with chronic primary insomnia received 4mg, 8mg, or placebo for 5 weeks. Found significant reduced in sleep latency at week 1 ($P=0.009$) and week 5 ($P<0.001$) and increase in total sleep time at week 1
- No withdrawal effect noticed

Ramelteon MOA



- Decreases evening alerting signal
- Enhances sleep onset



- Reinforces or shifts the timing of the circadian rhythm
- Influences regulation of circadian rhythms

Non-prescription Medications

- Alcohol
 - Frequently used to promote sleep but can be a major cause of sleep disruption
 - Causes decreased latency of sleep onset, increased slow wave sleep, and decreased REM sleep during the 1st part of night but as alcohol levels decline during the 2nd half of the night, increased amount of REM sleep rebound, sleep fragmentation, and early morning awakening occur
- Antihistamines
 - Associated with cognitive impairment, daytime drowsiness, and anticholinergic effects
 - No specific data show that antihistamines either improve insomnia or prolong sleep
 - Avoid in the elderly

- **Melatonin**

- Small, short-term trials report encouraging results on sleep quality and latency
- Potential lack of quality control in OTC melatonin, timing of ingestion, and appropriate dosing

- **Herbal preparation**

- Valerian, chamomile, hops, kava-kava, and passionflower are well-described sleep aids in herbal medicine
- Randomized controlled trials have been performed on valerian with efficacy and safety data being mixed or lacking

New Medication

- Suvorexant
 - 1st FDA approved dual orexin receptor antagonist
 - Targets wakefulness-promoting neuropeptides that regulate the sleep-wake cycle
 - Decreases sleep latency and increasing total sleep time
 - Usually taken on an empty stomach so that sleep onset is faster
 - Recommended to take when able to sleep for at least 7 hours continuously
 - Studies have found no significant efficacy or safety differences between elderly (65 yo and older) and non-elderly (agee 18 to 64 yo)
 - Common side effects: somnolence, fatigue, headache
 - Long-term data lacking

First line medications[†] for chronic insomnia in elderly

| Non-benzodiazepines (Z-drugs)* | Dose (mg) | Half-life (in hours) | Comment |
|--------------------------------|-----------|----------------------|---|
| 1 Zaleplon | 5-10 | 1-1.5 | Sleep-onset insomnia, can be given on waking during night |
| 2 Zolpidem | 5-10 | 1.5-2.6 | Sleep-onset insomnia |
| 3 Zolpidem controlled release | 6.25-12.5 | 2.8 | Sleep-maintenance insomnia |
| 4 Zopiclone | 3.75-7.5 | 2.5 | Sleep-maintenance insomnia |
| 5 Eszopiclone | 1-2 | 6 | Sleep-maintenance insomnia |
| Melatonin agonists | | | |
| 1 Melatonin [‡] | 1.5-6 | 0.5 | Sleep-onset insomnia |
| 2 Ramelteon | 8 | 1-2.6 | Sleep-onset insomnia |
| 3 Agomelatine [‡] | 25 | 2.3 | Sleep-onset and maintenance insomnia |
| Orexin antagonist | | | |
| 1 Suvorexant | 10-20 | 12 | Sleep-onset and maintenance insomnia |
| Histamine antagonist | | | |
| 1 Doxepin | 3-6 | 15 | Sleep-maintenance insomnia |

[†]All benzodiazepines are included in the Beers List (potentially inappropriate medication use in older adults); [‡]Evidence for efficacy in elderly is lacking;

*Evidence for efficacy up to 1 year

Common Disorders Related to Secondary Insomnia

- Obstructive Sleep Apnea
- Restless Leg Syndrome
- Rapid Eye Movement Disorder
- Circadian Rhythm Sleep-Wake Disorders

Obstructive Sleep Apnea

- Distinctive snoring pattern caused by intermittent airway collapse, periods of loud snoring or brief gasping followed by cessation of respiration lasting 20 to 30 seconds
- Leads to sleep arousals due to arterial O₂ desaturations
- Excessive daytime sleepiness, cognitive impairment that can include poor attention and recall, slowed response time, impairments in executive function
- Formal evaluation for OSA should be considered in elderly patients who exhibit typical symptoms
- Mainstay of therapy is positive airway pressure devices (CPAP)
- Hypnotics and other sedative medications worsen OSA

Restless Leg Syndrome

- Bubbly or creepy crawly sensation in legs, tingling, tickling, restlessness, stretching sensation in leg muscles that occurs during rest and relieved by movement
- Prevalence is 10-35% in >60 year olds
- Commonly seen in setting of iron deficiency, uremia, neuropathies, and cardiovascular disorders
- Serum ferritin <50 micrograms/L correlates with severe RLS symptoms
- Prevalence of RLS 15-40% of patients with uremia

Diagnostic Criteria for RLS/WED


| Criteria [†] | Comment |
|---|--|
| 1 Urge to move the legs ± unpleasant sensation in legs (<i>Dysesthesia of legs</i>) | Painful in 30-50% patients. Can also involve other body parts, but predominantly in legs |
| 2 Starts or worsens when one is inactive or at rest (<i>Quiscegence</i>) | Sensory symptoms are prominent during SIT |
| 3 Partial improvement by rest, till activity continues (<i>Movement responsive</i>) | At least some symptomatic relief is seen as soon as activity starts |
| 4 Only occur or worsens during evening or night (<i>Nocturnal</i>) | Ascertain circadian differences in response to symptoms to rest |
| 5 Not because of any other medical or behavioral condition (<i>RLS mimics</i>) | Differential diagnosis of RLS, improves diagnostic specificity |

[†]International Restless Legs Syndrome Study Group (IRLSSG) 2012 revised criteria; SIT: Suggested Immobilization Test; An easy to recall acronym URGE (urge to move the legs, rest makes it worse, get up and go to make it better, and evening and night times are worse)

- Non-pharmacological treatment: hot shower or massage before bedtime, regular sleeping and waking times, regular exercise, avoid caffeine/cigarettes/alcohol
- Antipsychotics, antiemetics, antidepressants, beta blockers, some anticonvulsants, and lithium are known to exacerbate RLS



Pharmacotherapy of RLS



| Drugs | Dosing (mg/day) |
|---|---|
| <i>Non-ergotamine dopamine agonists</i> | |
| 1 Pramipexole | Start at 0.125 mg, titrate every 5-days, effective dosage 0.125–0.75 mg |
| 2 Ropinirole | Start at 0.25 mg, titrate every 5-days, effective dosage 1.5–2.5 mg, maximum 4 mg |
| 3 Rotigotine | 0.5–3 mg |
| <i>Ergotamine dopamine agonists</i> | |
| 4 Pergolide† | Start at 0.05mg, titrate by 0.05mg every 2 to 3 days, effective dose 0.1 to 0.5mg, some require up to 1mg |
| 5 Cabergoline† | 0.5–2 mg |
| 6 Bromocriptine† | Start at 1.25 to 2.5 mg, increase every 1–2 weeks, up to 5–15 mg |
| <i>Dopamine precursors</i> | |
| 1 Levodopa† | 50–200 mg is effective, some may require up to 600 mg |
| <i>Anticonvulsants</i> | |
| 4 Gabapentin | 600–1200 mg, maximum 2700 mg |
| 5 Pregabalin | 150–450 mg |
| Carbamazepine | 100–400 mg |
| <i>Opioids</i> | |
| 6 Oxycodone | 2.5–15 mg |
| 7 Methadone | 5–40 mg |
| <i>Other agents</i> | |
| Clonazepam | Improves sleep, nor PLMS. 0.5–2 mg is usual dose |
| Clonidine | 0.1–1 mg |

†Not preferred because of higher rates of augmentation

Rapid Eye Movement Sleep Behavior Disorder

- Dream enactment behavior that ranges from simple to complex vocalizations and body movement during REM sleep
- No loss of muscle tone typically seen in REM sleep
- Idiopathic RBD is linked to neurodegenerative disorders, specifically Parkinson's disease, Lewy Body Dementia, and multiple system atrophy
- Patients with RBD are alert and immediately have vivid dream recall
- A 16-item Mayo Sleep Questionnaire can be used to screen for RBD and other sleep disorders
- All patients with dream enactment history should be screened for OSA, which can mimic RBD
- Although history may suggest RBD, polysomnography is often required for definitive diagnosis

- Injury-preventing techniques: modification of environment such as sleeping on floor, padding corners of furniture, keep the window and door locked at night, removing potentially dangerous objects, heavy curtains on bedroom windows to reduce sleep disruption, bed partner may be asked to sleep separately
- Discontinue medications known to exacerbate RBD: antidepressants, beta-blockers, tramadol, cholinesterase inhibitors
- If there is comorbid depression, bupropion is preferred
- Bed alarm that consists of a pressure sensor that get activated during dream enactment, plays a pre-recorded message telling patient its a dream, calming the patient so they can go back to sleep



Drugs used in treatment of RBD

| | Molecule | t _{1/2} (hour) | Dose (mg/d) | Comments |
|----|----------------|-------------------------------------|-------------|--|
| 1 | Clonazepam | 30-40 | 0.25-4 | 1 st line agent; suppresses phasic REM activity |
| 2 | Melatonin | 0.33-0.83 (dose/route dependent) | 3-12 | 2 nd line agent; restores REM sleep atonia; 30 min before bedtime |
| 3 | Zopiclone | 3.5-6.5 | 7.5 | Inconclusive/mixed results |
| 4 | Agomelatine | 1-2 | 25-50 | |
| 5 | Ramelteon | 2-5 | 8 | |
| 6 | Donepezil | 70 | 5-10 | |
| 7 | Rivastigmine | 1-2 | 6-12 | |
| 8 | Pramipexole | 8-12 | 0.5-1.5 | |
| 9 | L-dopa | 0.83-1.5 | 250-1250 | |
| 10 | Desipramine | 24 | 50-300 | |
| 11 | Sodium Oxybate | 0.5-1 | 2500-9000 | |
| 12 | Carbamazepine | 12-17 (repeated doses) | 400-1200 | |

Circadian Rhythm Sleep-Wake Disorders

Circadian rhythm sleep-wake disorders

| Disorder | Description |
|--|---|
| 1 Delayed sleep-wake phase disorder (DSWPD) | Sleep is delayed at least by 2 hours than usual along with a difficulty in falling asleep at the socially acceptable time. Uncommon in elderly. |
| 2 Advanced sleep-wake phase disorder (ASWPD) | Sleep occurs at least 2 hours prior to the usual times. Most common disorder in the elderly. |
| 3 Irregular sleep-wake rhythm disorder (ISWRD) | There is no clearly defined sleep-wake rhythm, with variable sleep and wake episodes. Seen in elderly patients with dementia. |
| 4 Non-24-Hour Sleep-Wake Disorder (N24SWD) (Free-running disorder) | The circadian pacemaker is not synchronous with the light/dark cycle leading to either insomnia or excessive sleepiness, depending on when sleep is attempted. Seen in blind individuals. |
| 5 Shift work disorder | Shifts in work schedules (e.g. night, early morning or rotating) cause decrease in total sleep time (typically by 1–4 hours) along with a subjective feeling of unrefreshing sleep. |
| 6 Jet lag disorder | The timing of endogenous circadian rhythm does not match with the time zone during long-distance travel. |

Advanced sleep phase

Normal sleep phase

Delayed sleep

Wake up
for school

6 pm 8 pm 10 pm Midnight 2 am 4 am 6 am 8 am 10 am Noon

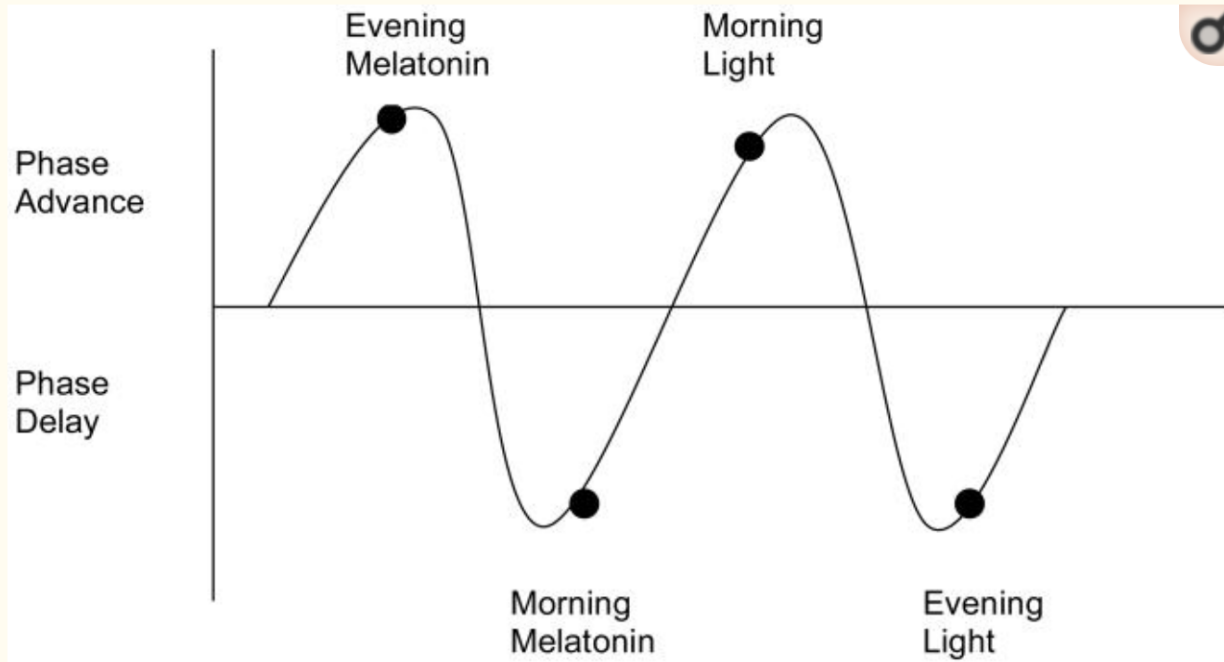


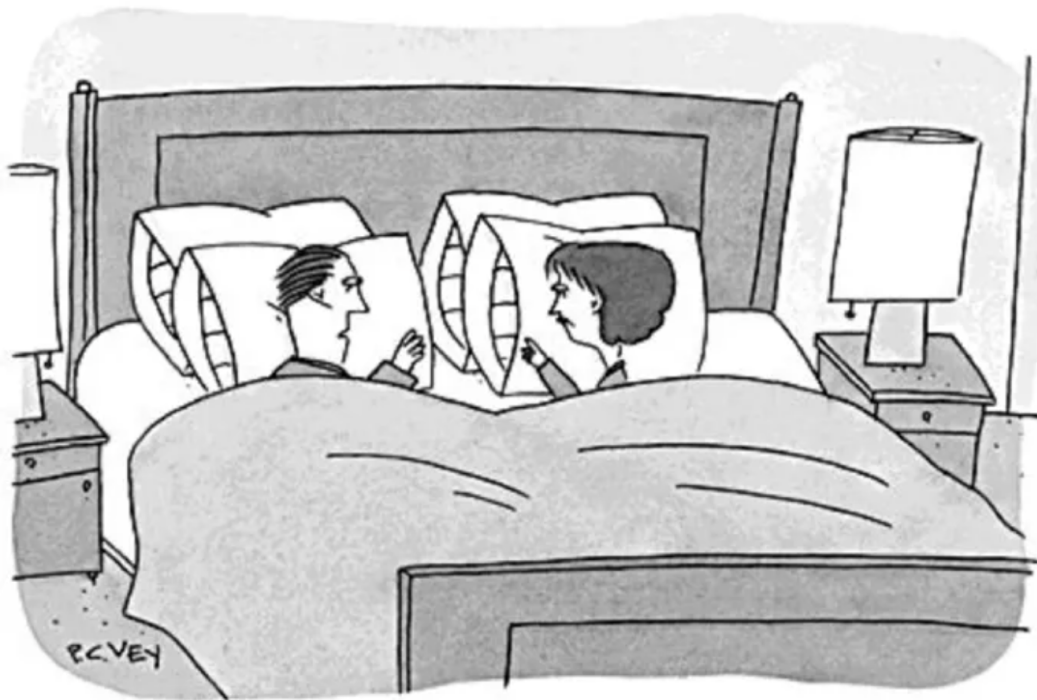
Figure 1

Schematic illustration of the human phase response curve (PRC) to melatonin and light. The black circles along the PRC indicate exposure to stimuli (e.g. light or melatonin). The position during which the stimulus occurs indicates whether the effect would result in a phase delay or advance of the circadian rhythm. Melatonin administration in the evening induces a phase advance, whereas given in the morning causes a phase delay. Morning light exposure results in a phase advance, while light exposure in the evening elicits a phase delay.

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Thank You



"I just don't feel right unless I get my normal eight hours of semiconscious drifting in and out of sleep."